Amendments to the Claims

Please amend the claims as follows:

1. (Currently amended) A polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding a specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising ~~at least one charged residue~~ a residue other than Gly at position 44, a Leu residue at position 45, and a Trp residue at position 47.

2. (Original) The polypeptide of claim 1 wherein the polypeptide is substantially monomeric.

3. (Currently amended) The polypeptide of claim 1, wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, ~~having a unique~~ said VH/VL interface comprising ~~at least one charged residue~~ a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

4. (Currently amended) The polypeptide of claim 3 wherein the selected phage clone is produced in E. coli as insoluble inclusion bodies and the ~~isolated~~ polypeptide isolated therefrom is subsequently refolded in-vitro and purified.

5. (Original) The polypeptide claim 3 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

6. (Original) The polypeptide of claim 1 wherein the specific antigen of interest is an immunoglobulin molecule.

7. (Original) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C comprises the consensus sequence: Gly-X-Ser-Pro-Gln, wherein X represents any amino acid.

8. (Original) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-Ser-Ile, and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp.

9. (Currently amended) The polypeptide of claim 3 [[1]] wherein the specific antigen of interest is tumor necrosis factor.

10. (Original) The polypeptide of claim 9 wherein the CDR3 sequence between residues 95 and 100C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys.

11. (Currently amended) The polypeptide of claim 3 [[1]] wherein the specific antigen of interest is Streptavidin.

12. (Original) The polypeptide of claim 11 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: His-Ala-Gln-Arg-Arg-Pro-Trp-Ile-Arg, and Glu-Asp-Pro-His-Pro-Gln-Arg-Gly-Tyr.

13. (Currently amended) A peptide capable of binding a specific antigen of interest, said peptide being derived from the randomized sequence of the CDR3 region of a polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding said specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising ~~at least one charged residue~~ a residue other than Gly at position 44, a Leu residue at position 45, and a Trp residue at position 47.

14. (Currently amended) The peptide of claim 13 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal

antibody without induced mutations or modifications in the original VH/VL interface framework residues, ~~having a unique~~ said VH/VL interface comprising ~~at least one charged residue~~ a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

15. (Original) The peptide of claim 13 wherein the peptide comprises 4-20 amino acids.

16. (Original) The peptide of claim 13 wherein the peptide comprises 7-15 amino acids.

17. (Original) The peptide of claim 13 wherein the specific antigen of interest is an immunoglobulin molecule.

18. (Original) The peptide of claim 13 wherein the specific antigen of interest is tumor necrosis factor.

19. (Currently amended) A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 3 [[1]], and a physiologically acceptable diluent or carrier.

20. (Original) A pharmaceutical composition comprising as an active ingredient the peptide of claim 13, and a physiologically acceptable diluent or carrier.

21-33. (Canceled)

34. (Currently amended) The pharmaceutical composition of claim 19 wherein the polypeptide is ~~substantially~~ predominantly monomeric.

35. (Currently amended) The pharmaceutical composition of claim 19 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, ~~having a unique~~ said VH/VL interface comprising ~~at least one~~

~~charged residue~~ a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

36. (Currently amended) The pharmaceutical composition of claim 35 wherein the selected phage clone is produced in E. coli as insoluble inclusion bodies and the ~~isolated~~ polypeptide isolated therefrom is subsequently refolded in-vitro and purified.

37. (Previously presented) The pharmaceutical composition of claim 35 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

38. (Previously presented) The pharmaceutical composition of claim 35 wherein the CDR3 sequence between residues 95 and 100C comprises the consensus sequence: Gly-X-Ser-Pro-Gln, wherein X represents any amino acid.

39. (Previously presented) The pharmaceutical composition of claim 35 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-Ser-Ile, and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp.

40. (Previously presented) The pharmaceutical composition of claim 19 wherein the CDR3 sequence between residues 95 and 100C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys.

41. (Previously presented) The pharmaceutical composition of claim 19 wherein the specific antigen of interest is Streptavidin.

42. (Currently amended) The pharmaceutical composition of claim 20 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, ~~having a unique~~ said VH/VL interface comprising ~~at least one charged residue~~ a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

43. (Previously presented) The pharmaceutical composition of claim 20 wherein the peptide comprises 4-20 amino acids.

44. (Previously presented) The pharmaceutical composition of claim 20 wherein the peptide comprises 7-15 amino acids.

45. (New) The polypeptide of claim 1 wherein the residue at position 44 is a charged residue.

46. (New) The polypeptide of claim 1 wherein the residue at position 44 is Lys.

47. (New) A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 1, and a physiologically acceptable diluent or carrier.